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THE SOCIAL RESPONSIBILITY OF THE SCIENTIST

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In the following article Professor Lederberg deals with dangers that might arise from the thousands of chemical food additives used in the United States. He suggests that biological scientists might do much to increase our knowledge of the possible harmfulness of these substances, and proposes that scientists consider themselves "vigilantes" in working to protect the general public health. It is of interest to note that he included the artificial sweetener cyclamate on his list of strongly suspected substances in his article, which was prepared *before* the government announced the ban on that substance.

The National Academy of Science estimates that 2,000 chemical substances are used as food additives. In order for a food additive in use before 1958 to be listed on the "generally recognized as safe" (GRAS) list of the FDA and be free of government regulation, the manufacturer merely must state that he considers the product safe; no laboratory testing is required. To remove the substance from the list the FDA may either go into court with laboratory evidence that the substance causes cancer in animals, or furnish compelling evidence of its injuriousness to man. Only two food additives, one of them cyclamate, have ever been removed from the GRAS list. The fact that the FDA, due to woeful understaffing and a serious lack of proper laboratory facilities, is incapable of testing very many questionable food additives, makes Dr. Lederberg's "vigilante" proposal all the more relevant.

Food Additives

Many of the brilliant intellectual talents of our era are closely engaged in investigations of nature whose long-term impact cannot be overestimated, and which cannot be impeded without great risk to the basic values embodied in the definition of man as "the rational animal." Nevertheless, many scientists are concerned over dissociation of their intellectual effort from the manifest and urgent problems of contemporary life. All too often, however, when they attempt to deal directly with major problems, they are frustrated by the slow pace at which national policies respond to the challenges of—for instance—peace, population, and pollution. The very scope of these challenges also tends to minimize the utility of the scientists' own individual expertise. In fact, on many issues the basic scientist holds little advantage over the average concerned citizen.

Without demanding these expressions of civic conscience, we suggest that many scientists could advantageously use their creative imagination to seek ways in which their special expertise could be applied to the possible solution of more obscure, if smaller, problems, or to the discovery and anticipation of insidious new ones. A biochemist, for example, may be uniquely aware of the toxicity of an environmental contaminant; a physicist might see parallels between his own theoretical work and the conditions for forming or dissipating smog; and so on. The individual creative mind can best determine its own locus of highest efficacy. Groups of scientists may be able to refine the anticipation of technical shocks—like synthetic substitutes for commodities imported from underdeveloped countries, or techniques of surveillance manipulation and intrusion on personal privacy—in time to plan for their amelioration.

In many sectors, small areas of science have been exploited as the foundations of major burgeonings of technology. Take for example the internal-combustion engine: We daily suffer from the consequences of the disharmony rampant in that technological growth—for instance, in the profligate poisoning of air with lead, nickel, and other smog-causing delicacies. Sensitive minds have reacted with a revolutionary movement that would seem to be aimed at taking us all back to the paleolithic age, a move that from the start is utterly unrealistic in terms of both the sacrifice of essential economic benefits of technology (food, shelter, health) and the loss of the kind of education and culture that thrive on economic surplus. It is also unrealistic in terms of the powerlessness that a savage culture would exhibit in comparison with the positive forces that technology can create. The net effect of the retreatist idea seems to be an alienation of life goals that threatens the very continuity of our culture. This is manifest, on the one hand, by the dropping-out and turning inward of the "counter-culture" movements; on the other, by a reinforcement of the illiberalism of the middle-class majority, exhibited in taxpayers' revolts against the support of education, of research, and indeed of all forms of social progress in the public sector.

I do not propose that the major blame for this conflict be heaped on the shoulders of the abstract scientist. However, it is evident that too often his abstraction has been a contributory factor—e.g., the denial of problem-solving techniques, or even of the existence of certain problems if they are beyond the reach of the methods of objective verification and reproducibility that are the core of the scientific method. In fact, I must condemn those social scientists who blindly have aped this kind of illusion of rigor much more than the physical scientists who have furnished the successful models of this approach in their own sphere. On the other hand, the scientist can still make an important contribution by exhibiting the success of compassionate rationality in seeking solutions to urgent human problems. For instance, the basic question of race-genetics should not be whether one race is genetically inferior. It should be whether we can isolate specific factors (genetic or environmental) that hinder successful acculturation, with a view to finding the remedies. In this light, the facts that at least 5 percent of blacks are heterozygous for an abnormal hemoglobin (the sickle cell trait), and that a great many poor children—black, brown, and white—are mentally retarded as a consequence of dysnutrition during fetal life, loom immensely larger than do scholastic debates about statistical studies of racial differences in genes "for intelligence." Everything we know about developmental genetics already tells us how milieu-dependent such genetic factors must be in any case, which deflates what little scientific interest inherently attaches to such debates. The other extreme, a passionate but unfactual insistence that individuals or racial groups are likely to be born with no significant difference in their biological adaptation to their present environment, is equally destructive to the actual solution of important problems.

I suggested earlier that a scientist could well apply his special knowledge in a kind of vigilance over contemporary affairs, to seek out specific opportunities where special knowledge suddenly becomes particularly relevant. If he investigates specific situations, he may be surprised how often he knows much more about a facet of some technical misapplication than almost anyone else: There are very few areas of technology where we begin to know enough to be justifiably complacent. The rule is that the basic work has never been done.

This widespread lack of basic work was dramatized for me recently when I realized that the safety of chlorine, as used in the sanitization of drinking water, swimming pools, utensils, dressing poultry, and so on, had never been carefully scrutinized in the United States since the chlorination of water supplies was first adopted 60-odd years ago. Today a large proportion of the drinking water in this country is chlorinated—a public-health measure which is undoubtedly the major bulwark against epidemics of typhoid fever, dysentery, and cholera. It would undoubtedly be conservative to say that millions of lives have been saved by its promulgation. In fact, concentrated urban settlement would be impractical without chlorination or some equivalent means of removing polluting bacteria from domestic water.

Chlorine was used for the treatment of sewage as early as 1835 (long before the work of Pasteur and Koch proved that infectious disease was an attack upon the human body by living microbes), the rationale being the dissipation of foul odors which were, for many years, blamed for contagion. Chlorine was first introduced into an American waterworks at Jersey City, New Jersey, in 1909, in response to potential contamination by sewage from nearby towns. The city demanded that the water company either install expensive filtration equipment or pay for diversion of the sewage. After considerable litigation the court found that the chlorination process was both safe and effective for the production of potable water.

It is difficult to reconstruct the arguments that would support, by contemporary standards, the safety of chlorination. Over the years a few tests of acute toxicity have shown that chlorinated water can be safely drunk in concentrations of 50 to 100 parts per million, by comparison with the 1 to 2 ppm generally required for water purification. And, during World War I, chlorine (under the name "Dakin's solution," the only available disinfectant for contaminated wounds) did what was generally considered a splendid first-aid job. But the only serious contribution to the subject that I could find did not appear until 1968, and that was by a German scientist, Dr. H. Drückrey. Drückrey, of the Max Planck Institute for Immunobiology at Freiburg, reared laboratory rats for seven successive generations on drinking water supplemented with 100 ppm of chlorine. The treated animals showed no obvious pathology, and no shortening of life-span as compared to that of the controls.

This is an impressive demonstration, but one which should have been made at least 50 years earlier because many theoretical suspicions concerning human uses of chlorine remain. For instance, no modern methods have been applied to test the claim that chlorine is rapidly dissipated when it reacts with organic material in the body's fluids. We have no clear picture

of where, how, or how quickly chlorine is converted into chlorine ions within the body, nor of intermediate products of that conversion. These days, what with the help of radioactive tracers, it should not be very difficult to find out.

What little we do know of the chemistry of chlorine reactions is portentous. It *should* at times react with nitrogenous groups from various sources to form substances which eventually reach and react with DNA, the genetic material of body cells—though probably only when used in badly contaminated waters needing heavy doses of chlorine.

Nobody knows for sure, because the reactions of chloride n with DNA have been remarkably little studied. What we have found out along these lines in our laboratories is this: We have confirmed that chlorine reacts very readily with DNA, and that it also inactivates purified DNA very rapidly. The data suggest that this inactivation process is actually the mechanism by which chlorine performs its intended function of killing bacteria and viruses. We also have considerable evidence, not yet completely conclusive, that chlorine causes mutations in the DNA of bacterial and yeast cells exposed to it.

This laboratory work does not necessarily mean that chlorine is a genetic hazard in man. It is conceivable that it is completely neutralized by -SH groups and other groups in proteins in the body fluids and in cell sap before it can react significantly with the DNA of tissue and germ cells. But this is no more than a reasonable supposition, and it might not be exactly right. We need more intense biochemical studies of the fate of chlorine introduced into the body. It is even more surprising that we have no epidemiological comparisons of districts which have, versus those that have not, intensely chlorinated their water supplies over periods of years.

In any case, the theoretical arguments, not yet experimentally resolved, about chlorine are at least as impressive as those about toxic residues, which have prevented radiation from being used for the sterilization of foods and water. However, radiation is an environmental factor to which there has already been almost too much scientific and public hypersensitization, at least by comparison with chemical environmental factors.

Very similar remarks could be made about a host of environmental factors. Rather than dwell in too much detail, I will offer a challenge to other scientists to read such references as "Water Quality Criteria," and food additives handbooks which contain long lists of compounds about whose biological effects little is generally known. One solitary reader might have the essential clue. As a teaser, I am providing a list (Table 1) of a few items which have caught my attention from the armory of food additives—substances which are intentionally added to foods and about which I believe reasonable questions can be asked concerning their effects on human health. These additives are not used out of malice; they are part of our economy of food technology, and they should not be condemned if they actually present no hazards. Do we know? And if we are unsure, how should the burden of risks be allocated?

Effective vigilance demands of the scientist more than his goodwill and energy. He must educate himself, more than in the past, about the social and technological realities he has overlooked. He also must find an institutional framework which will sustain the autonomy of his critical thinking—thinking which may eventually be imperiled by systems of research support confined to the contracting of specific results. That framework should also make some accommodation, in its system of prestige and rewards, for the contributions of critical vigilance as well as for those of topical analysis.

I am all too certain that many fellow scientists will discover

Table 1
A Selective Listing of Chemicals Used in Food Processing

acetal	hydrogen peroxide
acetone peroxide	nitrosyl chloride
allyl isothiocyanate	peracetic acid
axodicarbonamide	phenylethanol
benzoyl peroxide	sodium methyl sulfate
cyclamates	sodium nitrite
diethylpyrocarbonate	stannous chloride
ethylene oxide—methyl formate fumigant	sodium hypochlorite; chlorine; chloramine–T; chlorine dioxide
formaldehyde	

SOURCE: NRC publication No. 1274. (Items selected by J. Lederberg.)

their own special nightmares, on the basis of their personal expertise, when they review the long lists of approved additives. Of course, I realize that if the FDA had to give adequate scientific assurance about the absolute safety of every additive, we might starve to death while the necessary research was being done, and again when new insights into sources of peril emerged. Nevertheless, the food industry and the scientific community, as well as the government, should be sharpening their focus in dealing with these vital problems.

We should also think of more flexible legal and regulatory approaches to these problems. Abbott Laboratories* should not be charged with insincerity for having asserted its confidence that cyclamates were safe, but the cold, hard, retrospective fact is that the main risk was being borne by millions of consumers, not by the corporation. On the other hand, a government agency probably would have little to lose in responding to public arousal by banning a product before all the evidence was in.

Perhaps existing laws could be altered to provide for unconditional liability for the eventual hazard of a product when the FDA has certified a bill of particulars, for example about bladder cancer or mutation. An outfit like Abbott Laboratories would then have to back up its confidence by affirming its willingness to share the costs of ill results stemming from risks which prove to be not wisely taken on behalf of its customers. It might also be required to post an insurance bond, a move which would require the approval of what would most assuredly be an eagle-eyed and conservative insurance underwriter. In the long run this insurance (paid for by the consumer, any way one looks at it) would indirectly pay for important research on hazards, and for the development of safer alternatives—as well as encourage broader discretion by the purveyors of unproven products.

Protecting our genes from environmental damage is crucial

* Abbott Laboratories, it must be noted, dealt entirely correctly and prudently with transmitting the laboratory data on the basis of which cyclamates were eventually banned. These remarks are addressed to statements made by the management at a time when the safety of cyclamates was merely controversial.

for two reasons. One is parental concern for the health of children both living and planned-for. The other is the social burden of handicapped and retarded children who need not only our compassion but our material resources and the best of our technical skills. Furthermore, no self-respecting individual can be totally indifferent to his responsibility as a vessel of the species—as a trustee of a role in human evolution that answers to the most profound religious instincts.

Research geneticists are beginning to speak up more and more pointedly about their concern over genetic hazards. Not too many years ago, I was able to compartmentalize my own thinking to such a degree that I did not immediately grasp the relationship between an abstraction, like the statistics of "lethal mutations" in fruit flies, and the human impact of malformation in the newborn. The current generation of young scientists is less likely to miss such connections. However, we all have a basic responsibility to go beyond an emotional expression of concern, and to use it to energize the search for authentic scientific measures of potential hazards, and for means to neutralize them.

Unfortunately, just as many academic scientists have rediscovered the importance of relating basic science to human needs, the political establishment, which controls the purse strings, has turned away—perhaps in bafflement or resentment—from the difficulties that a truly careful use of scientific thinking uncovers about the world we make for ourselves. Unfortunately, nonresearch on (for example) new viruses arising in nature may conceal them from being promptly seen, but it will not make them disappear from the real world. Nor will it change the facts—only our insight into them—about the importance of viruses, or food additives, or drugs, as agents of genetic damage.

We biologists have still not done the job that badly needs to be done to assess the really important hazards of environmental chemicals in such areas as cancer, teratology (embryo damage), and mutation. We know that these effects are often associated with one another, so that when cyclamate derivatives are proven to break chromosomes, we should already be alert to

cancer potential. We may still make costly mistakes for lack of basic knowledge of chemical effects on cells.

We have a few fundamental tools today, especially in genetic studies of cultured human cells, that might begin to clear things up. We can also be looking more closely at the fundamental chemistry of DNA. For example, a somewhat surprising report that LSD forms chemical complexes with DNA in the test tube (see T. E. Wagner in *Nature* magazine, June, 1969) adds weight to claims that LSD breaks chromosomes. Even more recent work, indicating that the tryptamines, a whole class of related compounds which occur naturally in the brain, also react with nucleic acids, may unify these findings. After all, we have still to work out how these agents can affect brain function at all in such low concentrations, and nucleic acids in brain cells may well be their targets.

A group of geneticists and cell biologists, headed by Dr. Alexander Hollaender, retired director of biological research at the Oak Ridge National Laboratory, has organized a new "Environmental Mutagen Society" to help further the scientific understanding of these difficult problems. Such a group will fill a vitally useful function if it does nothing more than provide a channel for mutual communications among a wide range of separate disciplines: the DNA biochemist ordinarily does not have his attention directed to matters like outbreaks of chromosome diseases of newborns.

It is not likely that we will—and certainly we do not wish to—learn very much about genetic hazards from observations of catastrophes in human populations. We have a great deal of taxing work ahead in trying to set up scientifically valid and politically useful criteria for laboratory studies of these elusive but all-important hazards. This line of protective research should surely be the mandate of many more institutions than are now involved in looking for trouble in the human condition. I would not, however, want to rely too heavily on institutionalized answers to these kinds of problems—they are likely to become mere counterestablishments. After a flurry of resounding successes, they will have their own dogmas to defend. Instead, the responsibility must be diffused through the entire scientific–

academic community to provide innovative and unrelenting criticism, from every possible source of expertise and insight.

The project orientation of research support is fatal to this kind of vigilance, for it buys a scientist's time in order to accomplish a prespecified and negotiated task. So long as such projects are not too closely supervised, much critical and creative work is still possible with their indispensable support. The universities have, however, reached a state of such abject dependence on project funding that their academic freedom is in serious jeopardy. A reasonable answer would be a demand on the part of the university faculties and administrations that a modicum of *undirected* research is an essential adjunct of a system of project support. This could even be regarded as an indispensable "overhead" item, to sustain the environment of a free university that, it is generally agreed, is most conducive to effective basic research. Without some room for a maneuver of this kind, the very abundance of centralized support for university research may stifle the scientists from the full exercise of their obligation of vigilant criticism. And a period of recession after vigorous growth is even more perilous.